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Etiological structure of the urinary system infections, its dynamic, dependence on patients sex and relation with resident urine microflora among inhabitants of Chernivtsi region and town of Chernivtsi

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ABSTRACT

During 2009 - 2013 years 2828 urine samples of the patients (2432 – children's and 396 - adults) of the medical network of the Chernivtsi region were investigated with bacteriology method with purpose of verification of the diagnosis «Infections of the urinary system»; 801 strains of bacteria and fungi were isolated as etiological agents. The main etiological role of the *E. coli* and enterobacteria family in general was demonstrated. It was revealed, that etiological structure of the infections of the urinary system and the content of the residential urine microflora depend on the patient's sex. As causative agent of the infections of the urinary system, *E. coli* has been isolated more frequently of the urine samples of female patients. In contrary, *Proteus* spp. has been isolated more frequently of the urine samples of male patients. As a part of the urine resident microflora, *E. coli* strains were isolated of the female urine samples more frequently.

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1. Introduction

Infections of the urinary system (IUS) – is a group of heterogeneous diseases that are combined by presence of infectious factor in the urinary tract and / or kidney, which causes inflammation in them (Kolesnyk et al. 2007; Stepanova et al. 2005). They occupy one of the leading places among infectious diseases in outpatient practice as well as in hospital (Rafalsky et al. 2006). Annual population surveys show a steady growth of the cases of IUS amongst children. Among infants (first three years of life), this pathology is more common than acute respiratory infections (Korovina et al. 2002; Serova, Paunova 2007). The incidence of acute cystitis in women is second only to respiratory infections (Sidorenko, Ivanov 2005).

IUS also occupy a prominent place among nosocomial infections. For example, among patients in critical condition, their share could reach 40%. According to cumulative data of the foreign researchers they occur in 6-8% of patients of the intensive care departments (Grabe (Chairman), Bishop, Bjerklund-Johansen et al. 2012; Zorkin 2007).

Regarding the etiology of IUS among experts in this field the unanimous opinion on the leading role of enterobacteria dominates (Grabe (Chairman), Bishop, Bjerklund-Johansen et al. 2012; Kolesnyk et al. 2010; Ramakrishnan, Scheid 2005). And among the latter the strains of *E. coli* are isolated the most often - in 70-95% of cases of uncomplicated IUS (Korovina et al. 2002; Loran, Sinyakova, Kosova 2005; Rafalsky et al. 2006; Romanenko, Stepanova, Rudenko et al. 2013; Zorkin 2007). In the overwhelming number of cases (95%) of uncomplicated IUS the causative agent is presented by one strain (Loran, Sinyakova, Kosova 2005). However, in the case of nosocomial IUS the range of causative agents is wider and includes both Gram-negative and Gram-positive bacteria (Kolesnyk et al. 2007; Kolesnyk et al. 2010; Zorkin 2007). Attention is drawn to the fact that the etiologic structure of IUS may vary in different geographical regions (Korovina et al. 2002). It should be also taken into account that under bacteriological examination of the urine of patients with IUS in 0.4-30.0% of cases abnormal microflora was not isolated (Loran, Sinyakova, Kosova 2005).

2. Purpose of the Study

Purpose of the Study is to set the current etiologic structure of the IUS, its dynamic, dependence on patient gender and relations with the urine resident microflora among Chernivtsi region population.

3. Material and methods.

During 2009 - 2013 years 2828 urine samples of the patients of the medical network of Chernivtsi region were investigated with bacteriology method with purpose of verification of the diagnosis «infection of the urinary system» (IUS).

S.epidermidis) , enterococci (*E.faecalis*), streptococci (*S.pyogenes*), yeast fungi (*C.albicans*). Based on the taxonomic proximity all strains that were isolated in etiologically significant quantities were divided into 5 groups: I gr. – Enterobacteriaceae (*Proteus* spp. excluded); II gr. – *Proteus* spp.; III gr. – *Pseudomonas* spp.; IV gr. – Gram-positive cocci; V gr. – Yeast fungi.

In the study the fourth group was the most diverse, because it consisted of representatives of coccal flora (staphylococci, streptococci and enterococci). This was due to the fact that these strains of pathogens were isolated in a very small number of cases which did not allow making analysis by different genera.

During 2009 - 2013 years 801 strains of bacteria and fungi were isolated as etiological agents from urine. In the overwhelming number of cases, only one etiologically significant strain was isolated from one sample of urine.

The data were processed statistically using the Excel program and the methods of variation statistics. Distribution of surveyed patients accordingly to their age and sex is shown in the table 1.

Table 1. Distribution of patients examined during 2009-2013 years accordingly to the age and sex

Age group		The total number of analyses performed	Sex of the patient	
			male	female
children	up to 3 years	632	207	425
	4 - 6 years	604	164	440
	7 - 14 years	887	303	584
	15 - 18 years	309	119	190
adults	19 - 35 years	223	39	184
	36 - 45 years	68	13	55
	46 - 65 years	89	26	63
	older 65 years	16	3	13
In sum		2828	874	1954

4. Results and discussion.

Among the patients studied the majority were children under the age of 15 years with peak values per age group of 7 - 14 years. The dependence on sex is notable among the examined patients. In all examined age groups the number of female patients exceeded the number of male patients in 1.6 - 4.7 times. The maximum difference was observed among the age groups of adults (19 - 35 years; 36 - 45 years and older than 65 years (Fig. 1).

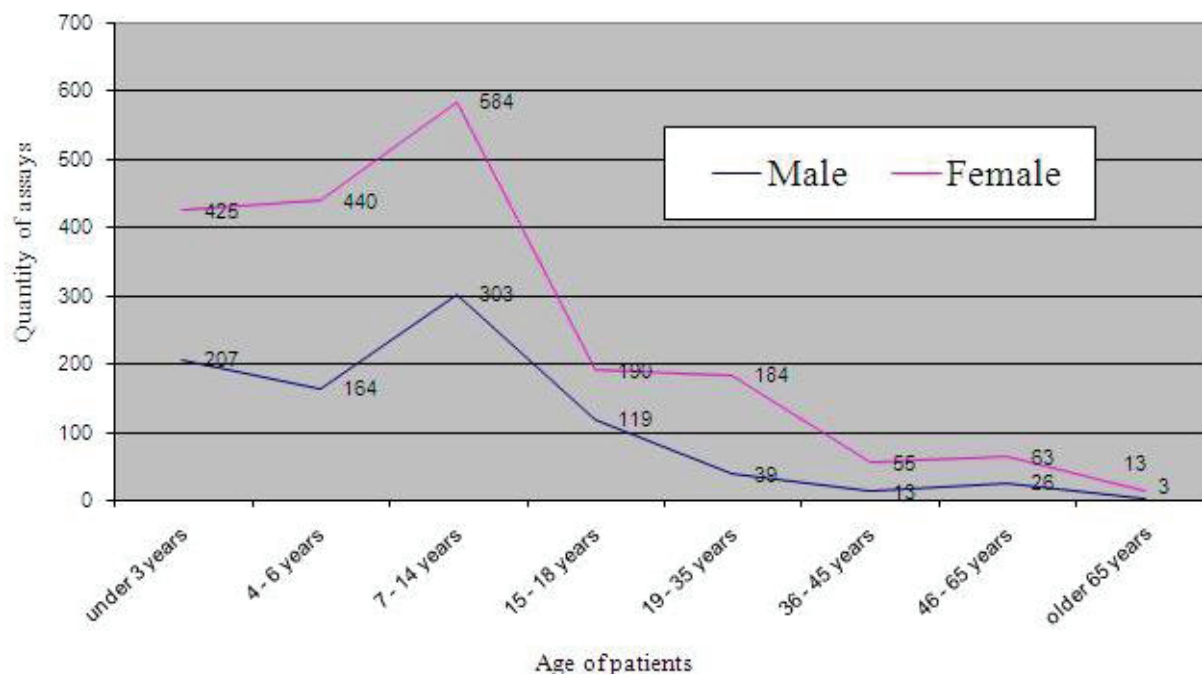


Fig. 1. The age and sex distribution of bacteriological assays conducted among patients with infection of the urinary system during 2009-2013.

Dynamics of frequency of isolation of etiologically significant strains of bacteria and fungi from the urine of the patients also revealed dependence on the age and sex of patients. In the age group surveyed children under 3 the percent of isolation of IUS causative agents among boys was higher than among girls. In all other examined age groups the percentage of isolated pathogens in female patients was higher.

In general, for both sexes it was observed a gradual decrease in the percentage of isolated IUS causative agents from the youngest age group up to 15 - 18 years inclusive. At the same time it should be noted a significant difference in percentage of isolated pathogens between adolescent female patients and their peers. In the older age groups of adults increased frequency of isolation of the etiologically significant strains was observed (Fig. 2).

Etiological structure of the urinary system infections, its dynamic, dependence on patients sex and relation with resident urine microflora among inhabitants of Chernivtsi region and town of Chernivtsi

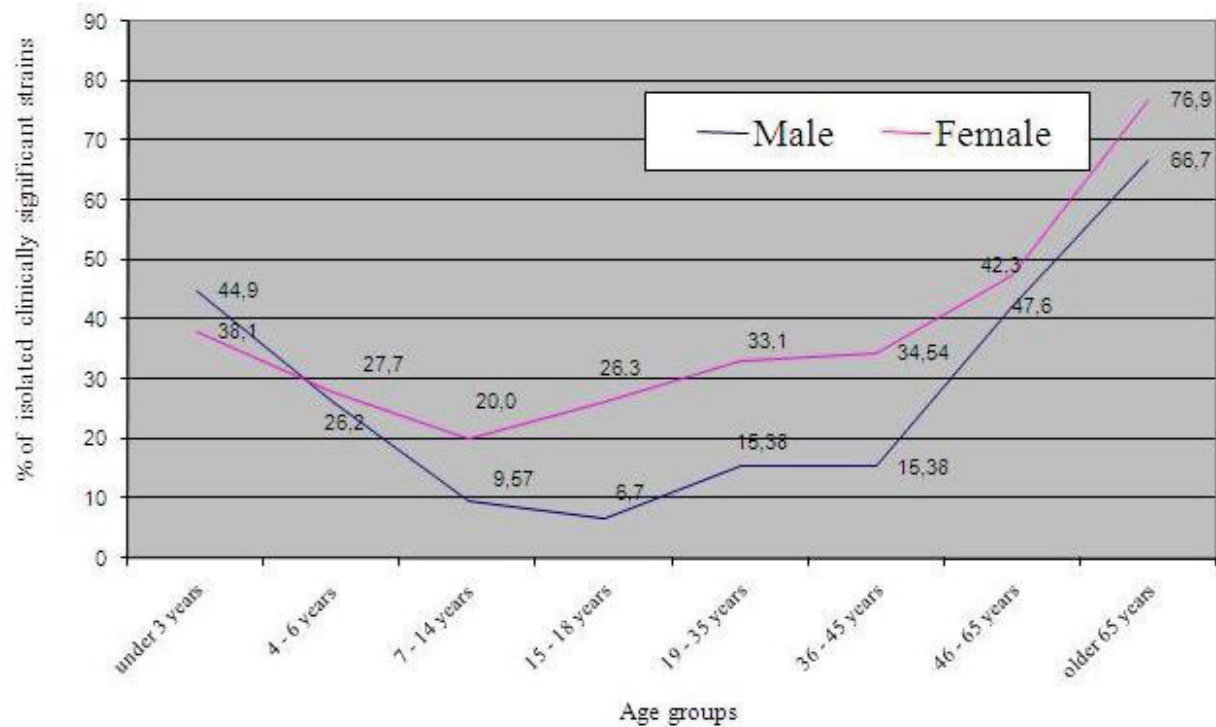


Fig. 2. The age and sex distribution of the clinically significant strains of bacteria and fungi isolated from patients urine samples

Among the IUS pathogens, isolated in 2009 - 2013 years, Enterobacteriaceae spp. (excluding *Proteus* spp.) was on the first place – from 63.6% to 76.6% of total cases isolation etiologically significant microflora. *Proteus* spp. was on the second place – from 10.27% to 15.58%. *Pseudomonas* spp., Gram-positive cocci and fungi were being isolated from the urine with approximately equal frequency: *Pseudomonas* spp. – 5.48-10.39%, Gram-positive cocci – 3.05-9.58%, yeast fungi – 3.59-7.14% (Fig. 3).

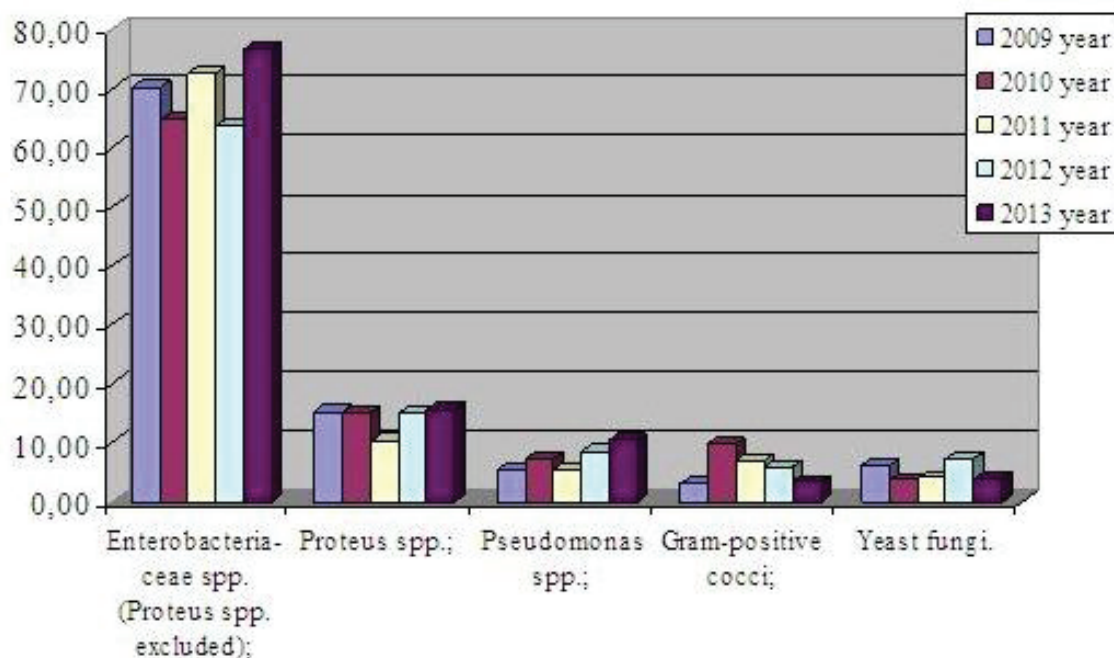


Fig. 3. Etiological structure of urinary system infections in the population of Chernivtsi region

The results are consistent with findings of researchers (Grabe (Chairman), Bishop, Bjerklund-Johansen et al. 2012; Kolesnyk et al. 2010; Korovina et al. 2002; Ramakrishnan, Scheid 2005), who have pointed out to a key role of the Enterobacteriaceae spp. in the etiology of IUS. However, the question of dependency of the IUS etiological structure on the patients' sex in the scientific literature is not highlighted enough.

Analysis of the results revealed age and gender dependence of the IUS etiological structure. Frequency of isolation of the Enterobacteriaceae spp. (excluding Proteus spp.) was significantly higher while examining female patients, except for the oldest age group. For examined three age groups the difference was statistically significant, namely: for children of 4 - 6 years ($n = 105$, Student's t-test value = 2.20, $p < 0.05$); children 7 - 14 years ($n = 113$, Student's t-test value = 2.36, $p < 0.05$) and for adults 36 - 45 years ($n = 12$, Student's t-test value = 5.48; $p < 0.001$). Within the same sex the frequency of isolation of the Enterobacteriaceae spp. (excluding Proteus spp.) revealed a small dependence on the age of patients. The sharp rise in this index was observed only in patients older than 65 years old (Fig. 4).

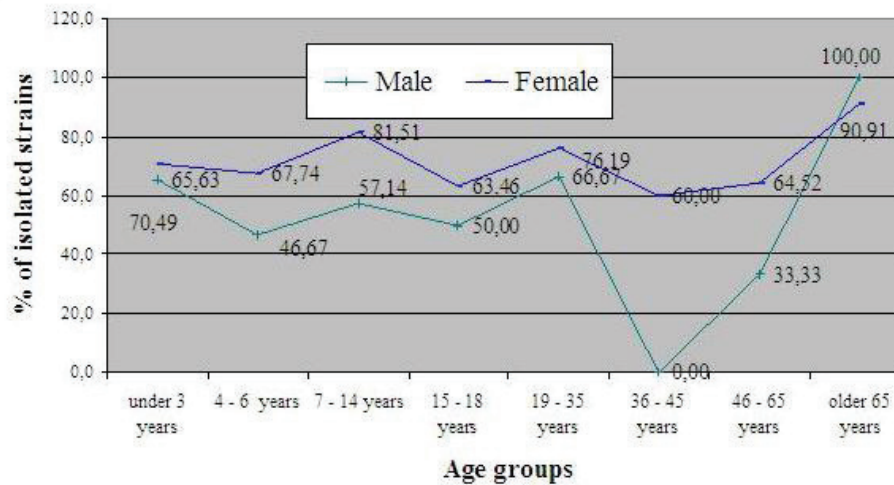


Fig. 4. Dynamics of isolation of Enterobacteriaceae spp. (except Proteus spp.) from the urine of patients with urinary tract infection in different age groups

For Proteus spp. reversed pattern appeared. Among patients under 35 the percent of Proteus spp. isolated of urine was higher among male patients. The difference was statistically significant for children of 4 - 6 years only ($n=34$, Student's t-test value = 2.80; $p < 0.01$). In the age groups over 35 Proteus spp. were isolated more often from the urine of female patients. It is noteworthy that for patients of both sexes the frequency of Proteus spp. isolation decreased with increasing the age of the patient (Fig. 5).

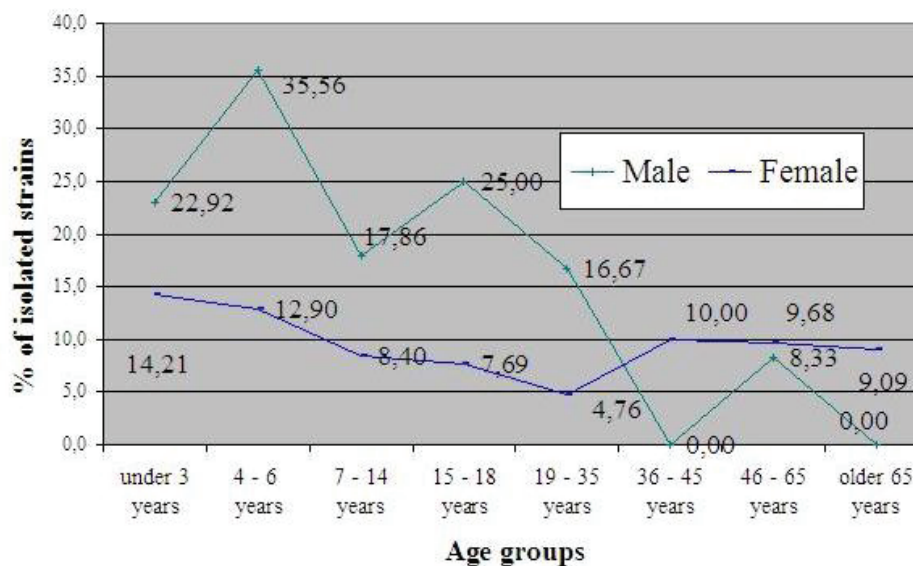


Fig. 5. Dynamics of isolation of Proteus spp. from the urine of patients with urinary tract infection in different age groups

Frequency *Pseudomonas* spp. isolation from the urine of patients of both sexes under age 35 years was about the same; and it was changing a little in the different age groups. The sharp rise of this index was registered only among male patients at mature age and older. However, in these cases the difference compared with the corresponding figures for female patients was not statistically significant. It can be explained by the small total number of cases of the pathogen allocation. For the patients of both sexes in the age group of 36-45 only two cases of isolation were registered, and in the age group 46-65 years - 8 cases (Fig. 6).

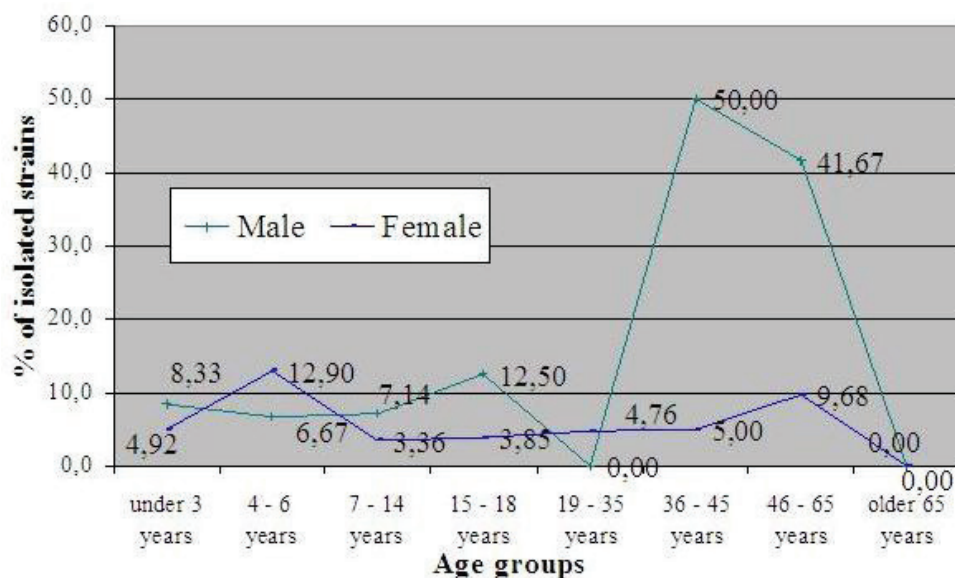


Fig. 6. Dynamics of isolation of *Pseudomonas* spp. from the urine of patients with urinary tract infection in different age groups

For Gram-positive cocci and yeast fungi clear relationship between age, gender and frequency of their isolation of urine as IUS pathogens was not found.

During the study the hypothesis was formulated: if the etiological spectrum of pathogens IUS was dependent on the sex of the patients, then the resident microflora urine may show the similar patterns. Moreover, namely the resident microflora at favorable factors for it (for example reduction in local or general immune defense, urodynamics malfunction) may cause the IUS.

In cases, when only the resident microflora was isolated from urine, from one to four species of bacteria and fungi were found in one urine sample. The average values of isolated strains per one analysis varied by different years of observations (2009-2013 yy.) - from 1.6 to 1.8. Coagulase-negative strains of staphylococci were isolated the most frequently, *Corynebacterium* spp. was on the second place and enterococci was on the third one (Fig. 7).

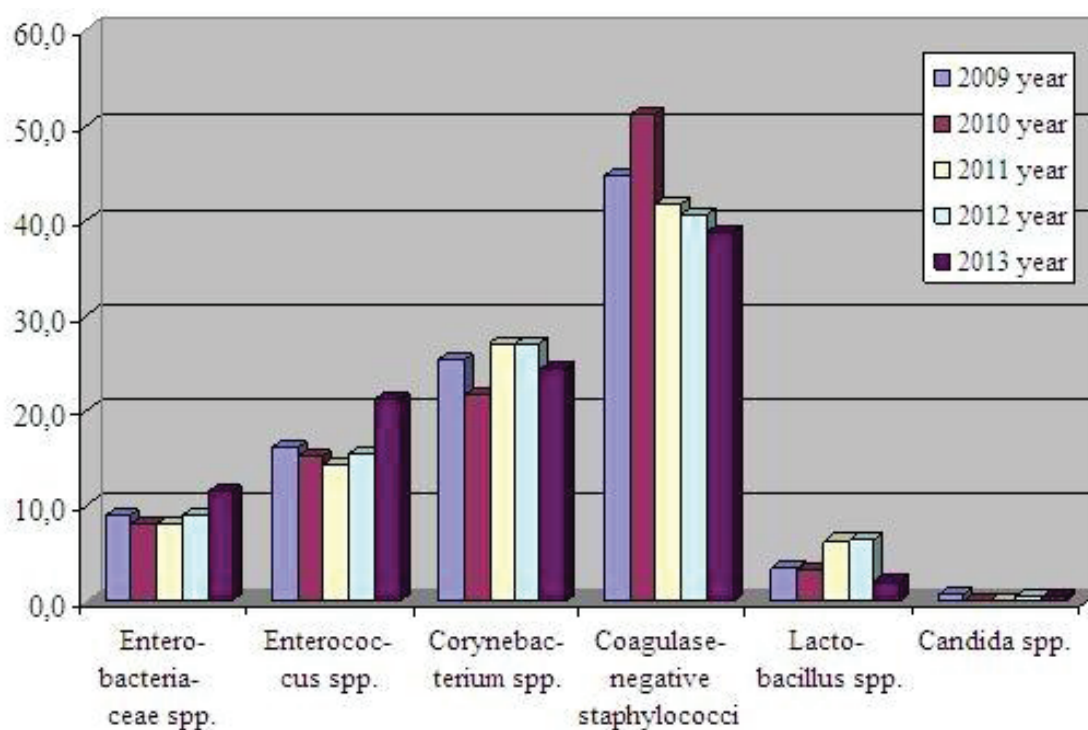


Fig. 7. The structure of the urine resident microflora of the Chernivtsi region population

Statistically significant differences between the sexes in the frequency of isolation of *Corynebacterium* spp. and *Enterococcus* spp. were not found. Coagulase-negative strains of staphylococci were isolated more frequently from the male patients ($n=1139$, Student's t -test value = 3.18; $p<0.001$). *Lactobacillus* spp. were isolated only from urine of female patients, it is explained by the generally known fact of their belonging to the resident microflora of female genital tract. There were single cases of isolation from urine *Micrococcus* spp., *S. viridans*, *Bacillus* spp., non pathogenic *Neisseria* spp. Frequency of isolation of yeast fungi of the genus *Candida*, as a part of the resident microflora varied from 0% to 0.7% during different years of observations. Differences between the sexes with this indicator were also not revealed.

Enterobacteriaceae spp., as a part of the urine resident microflora, took the fourth place by frequency of isolation. But based on the fact that the most frequent causative agent of the IUS are just *Enterobacteriaceae* spp. (Kolesnyk et al. 2010; Ramakrishnan, Scheid 2005), the isolation frequency dynamics of those strains among patients of different age groups was investigated. Based on the results of observations, frequency of isolation of *Enterobacteriaceae* spp. for patients of both sexes has tendency to decrease with increasing age of patients. This group of bacteria was isolated more often from female patients under 18. For the three age groups, the difference was statistically significant: for children up to 3 ($n=86$, Student's t -test value = 3.14; $p<0.01$), for children of 7 – 14 ($n=63$, Student's t -test value = 5.05; $p<0.001$) and adolescents ($n=21$, Student's t -test value = 2.70; $p<0.05$) (Fig. 8).

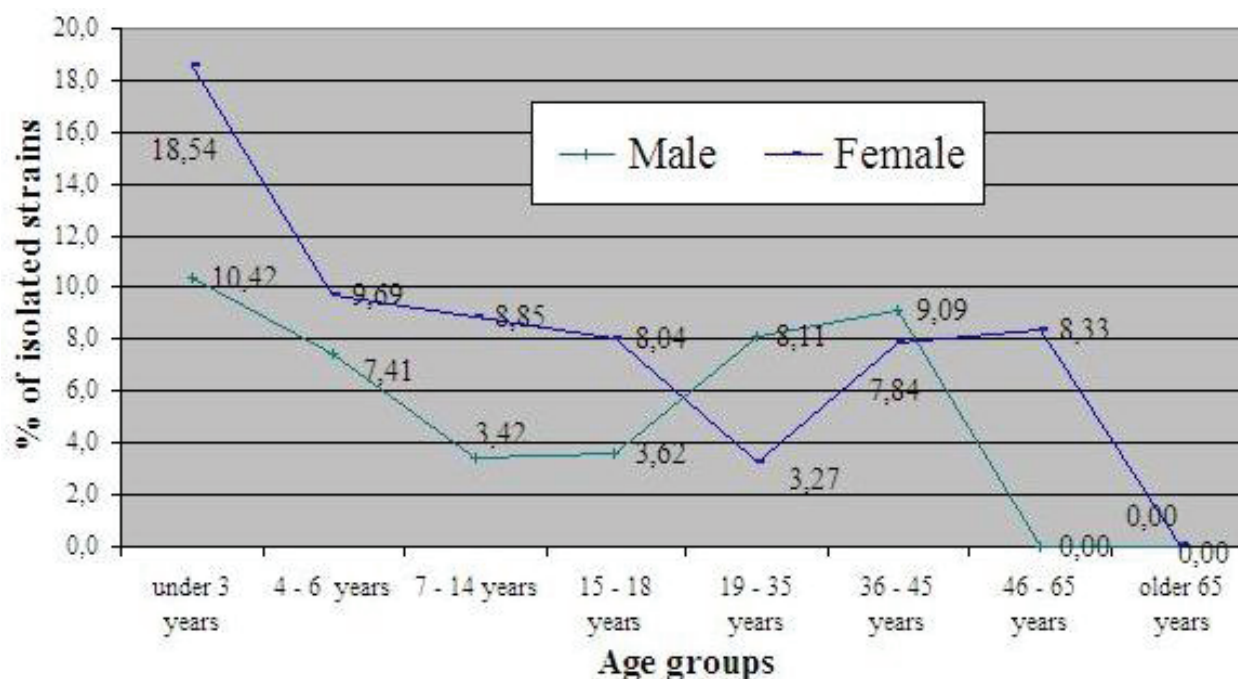


Fig. 8. The dynamics of Enterobacteriaceae spp isolation as a part of the urine resident microflora among different age groups

Differences between the sexes in the frequency of Enterobacteriaceae spp. isolation as part of the resident microflora undoubtedly underlie the gender differences in the frequency of their isolation as the etiologic agent of the IUS.

Enterobacteriaceae spp. belong to obligate resident intestinal microflora, as well as enterococci. However, the frequency of isolation of enterococci, in contrast to Enterobacteriaceae spp., was almost identical in patients of both sexes. The reason for the detected differences may be due to different mechanisms of interaction of enterobacteria spp. and enterococci with uroepithelium female and male urinary tract (Romanenko, Stepanova, Rudenko et al. 2013).

Conclusions.

1. For the epidemiology and etiology of urinary tract infections among the population of town Chernivtsi and Chernivtsi region the signs are common for this pathology: the number of female patients is predominant the number of male patients in all age groups; among children up to 3 the percentage of isolation etiologically significant microorganisms from urine is higher among boys, and in all other age groups etiologically significant microflora is isolated more often from female patients; the main etiological agent of infections of the urinary system are Enterobacteriaceae spp..

2. Between the sexes there are differences in the species composition of the urinary system infection agents. Among female patients *E.coli* is isolated more often and bacteria of the genus *Proteus* - among male patients.

3. The differences between sexes in the composition of the resident microflora of urine do exist. Among female patients the strains of *E.coli* are isolated more often, which may be a prerequisite for the top spot of the pathogen in the etiology of infections of the urinary system among women and girls.

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